

## **REMARKS**

### **Status of the Claims**

Claims 1-28 are pending in the present application. Claims 9-28 are withdrawn from consideration as directed to a non-elected invention. Claim 1 is amended for clarity. No new matter or new issues are entered by way of this amendment. Reconsideration is respectfully requested.

### **Election/Restriction**

The Examiner states that a complete reply to the final rejection must include cancellation of non-elected claims, *see Office Action*, page 2. Applicants submit that the requirement to cancel non-elected claims is improper at this stage of prosecution. Cancellation is proper only when the application is otherwise in condition for allowance, *see* MPEP § 8.03. Accordingly, Applicants respectfully request withdrawal of the Examiner's requirement.

### **Objection to the Claims**

Claim 1 is objected to for specifying "a food or the food ingredient." Claim 1 is amended to correct this informality. Applicants respectfully request withdrawal of the objection.

### **Issues Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-8 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for recitation of the equation, *see Office Action*, page 3. The Examiner states that the equation does not indicate the order in which the calculation is to be done.

In an effort to expedite prosecution, the equation described in claim 1 is amended to specify:

$$\frac{F_s}{L_s} \times \frac{L_o}{F_o} \times 1,000,000$$

In view of the foregoing amendment, Applicants believe the rejection is overcome and respectfully request withdrawal.

**Issues Under 35 U.S.C. § 103(a)**

*Claims 1-3, 6, and 8*

Claims 1-3, 6, and 8 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Publication No. 2003/0207298 to Hirao *et al.*, (“Hirao”) in view of Haugland *et al.*, *Molecular and Cellular Probes*, 1999, 13:329-341, (“Haugland”), *see Office Action*, pages 4-8 . Applicants respectfully traverse.

**Basis of the Rejection**

The Examiner states that Hirao describes PCR-based methods for detecting a target plant genus in a food ingredient. According to the Examiner, Hirao teaches methods that are especially suitable for detecting the presence of allergenic plants, such as plants of the genus *Fagopyrum*. The Examiner admits that Hirao does not describe performing quantitative real-time PCR using fluorogenic probes to determine DNA copy number from the plant genus to be tested. The Examiner further admits that Hirao does not describe that the disclosed PCR detection methods use a sample for correction comprising a known amount of a standard plant sample or that a known amount of the standard plant is added to the food ingredient or food sample to be tested, as required by claim 1.

However, the Examiner believes that Haugland remedies the deficiencies of Hirao. According to the Examiner, Haugland describes a method, which comprises adding a known amount of a standard fungal sample to a test sample and measuring the copy number of the standard fungal species and the copy number of the target fungal species by real-time PCR. According to the Examiner, Haugland further describes that the method comprises preparation of a sample for correction, *i.e.* a calibrator, containing a known amount of the target fungal species and a known amount of the standard fungal species and then determining the copy number of the target and standard fungal species by real-time PCR.

The Examiner believes that an ordinary artisan would have applied the teachings of Haugland to the method of Hirao since an ordinary artisan would have been motivated to substitute real-time PCR with the fluorogenic probes as taught by Haugland for the conventional PCR amplification and detection method taught by Hirao. The Examiner further alleges that an ordinary artisan would also have been motivated to utilize a sample for correction, comprising a

standard plant sample, and perform the associated analysis as taught by Haugland, in order to obtain the ability to control for sample to sample variations in DNA extraction efficiency.

The Examiner Has Failed to Present a *Prima Facie* Case of Obviousness

When determining whether a claim is obvious, an examiner must make "a searching comparison of the claimed invention including all its limitations with the teaching of the prior art." *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995). Thus, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)). Moreover, as the Supreme Court recently stated, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

In addition, the Examination Guidelines for Determining Obviousness Under 35 U.S.C. § 103 in view of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* state that, having undertaken the factual inquires of *Graham*, a rejection under 35 U.S.C. § 103 may be supported by one or more rationales, including combining prior art elements according to known methods to yield predictable results. The above-noted rationale requires predictability in the art and/or a reasonable expectation of success, and the Examiner must consider objective evidence, which rebuts such predictability and reasonable expectation of success. This objective evidence or secondary considerations may include evidence teaching away from the currently claimed invention. *Id.*

*The combination of Hirao and Haugland does not teach all of the elements of the instant claims*

In the response filed on April 29, 2009, Applicants described the Hirao disclosure. The April 29, 2009, remarks regarding Hirao are incorporated herein. Applicants further submit that Haugland does not remedy the deficiencies of Hirao. The method of Haugland concerns a method for quantifying fungus in air samples collected from, e.g., a room. Specifically, Haugland describes quantifying the number of cells of *S. chartarum*, which is one type of fungi, in an indoor environment by a PCR method, see page 329 and abstract of Haugland. In particular, the Haugland method comprises the following steps:

1) preparing two samples: i) a calibrator sample, wherein *S. chartarum* and *G. candidum* are used as a standard and mixed in a predetermined ratio, and ii) a test sample, wherein a known quantity of *G. candidum* is added to an unknown quantity of *S. chartarum*,

2) extracting DNA from the above two samples, respectively,

3) practicing a quantitative PCR using a primer set for detecting *S. chartarum*, and a primer set for detecting *G. candidum*, with the above DNA extracted from each of the samples, as a template, and

4) determining the number of cells of *S. chartarum* present in the test sample by comparing the cycle threshold (Ct\*) of *S. chartarum* DNA in both samples, and compensating for the variability in DNA extraction and amplification efficiencies with the use of the Ct\* of *G. candidum* DNA in both samples.

Ct\* refers to the cycle number at which the amplification curve crosses this threshold.

In contrast to Haugland, the claimed invention describes a method of quantifying plant DNA belonging to a specific plant genus, such as buckwheat, in a food or food ingredient, by a PCR method. The claimed method comprises the following steps:

(I) preparing two samples; a sample for correction, wherein i) a sample derived from the specific plant genus to be detected and a standard plant sample are mixed in a predetermined ratio, and ii) a test sample, wherein the food or food ingredient to be examined and a standard plant sample are mixed in the same amount as the above sample for correction,

II) extracting DNA from the above two samples, respectively,

III) practicing a quantitative PCR using a primer set for detecting the sample derived from the specific plant genus to be detected and a primer set for detecting the standard plant sample, with the DNA extracted from each of the samples for correction and the test sample as a template,

IV) determining the copy number of the DNA derived from the standard plant (Lo) and the copy number of the DNA derived from the specific plant genus (Fo) for the sample for correction, and determining the copy number of the DNA derived from the specific plant genus (Fs) and the copy number of the DNA derived from the standard plant (Ls) for the test sample, and

V) calculating the amount of the plant belonging to the specific plant genus contained in the food or food ingredient using the above copy numbers according to the following equation:

Amount of plant belonging to specific plant genus (ppm (μg/g))=

$$\frac{F_s}{L_s} \times \frac{L_o}{F_o} \times 1,000,000$$

Initially, Applicants note that the subject to be quantified in the claimed method is fundamentally different from that of Haugland. The subject of quantitative measurement in the claimed method is a plant belonging to a specific plant genus, *e.g.*, the genus *Fagopyrum*, *Arachis*, *Triticum*, or *Glycine*, contained in a food sample. In contrast, the subject of quantitative measurement in Haugland is a fungus, which is contained in a sample due to trapping environmental, floating, substances into a solution. Accordingly, the quantitative measurement of the present invention is much more difficult than that of Haugland, since a food consists of materials including a variety of components.

Secondly, although steps (1) to (3) of Haugland are substantially similar to steps (I) to (III) of the claimed invention, step (4) of Haugland is completely different from steps (IV) and (V) of the present invention. Haugland does not teach or suggest the technical concept depicted in steps (IV) and (V) of the present invention. That is, Haugland fails to teach or suggest

**determining the copy numbers of each DNA and calculating the amount of the plant belonging to the specific plant genus contained in a food by applying said copy numbers to the specified equation.**

Hirao also does not disclose or suggest the technical concept of steps (IV) and (V) of the claimed method.

In contrast to the cited references, the claimed method describes the copy number of the DNA derived from the standard plant (Lo) and the copy number of the DNA derived from the specific plant genus (Fo) for the sample for correction. The copy number of the DNA derived from the specific plant genus (Fs) and the copy number of the DNA derived from the standard plant (Ls) for the test sample, are also described and are determined by a calibration curve. The method for preparing the calibration curve is described in detail in the present specification, *see* examples in the instant application. Such a technical concept is not disclosed or suggested in Haugland or Hirao.

*Haugland teaches away from the instant invention*

Haugland further teaches that the prior art method, which uses calibration by the addition of *G. candidum*, as described above, did not improve the accuracy of Haugland's method in comparison to the method without such calibration, *see* page 330, right column, lines 3 to 11 of Haugland.

Accordingly, improved accuracy could not be attained by the correction, (calibration), described in step (4) of Haugland. That is, Haugland teaches that correction is not necessary. Accordingly, the cited art teaches away from the correction step as specified in the instant claims.

Applicants note that correction is unnecessary in Haugland because the subject to be quantified in this reference is a fungus, contained in a sample prepared by trapping environmental, floating, substances into a solution. In contrast, correction is necessary in the present invention, since the DNA content of a food sample affects the accuracy of quantification, in addition to affecting DNA extract efficiency and PCR inhibition.

Based upon the foregoing, the claims are not obvious in view of the cited references. Accordingly, withdrawal of the rejection is respectfully requested.

*Claims 4 and 5*

*Hirao, Haugland, and Palacios*

Claims 4 and 5 are rejected as allegedly obvious over Hirao in view of Haugland and Palacios *et al.*, *Molecular Phylogenetics and Evolution*, 2000, 14:232-249, ("Palacios"), *see Office Action*, pages 8-9. Based upon the following, Applicants respectfully traverse.

As noted above, Hirao and Haugland fail to teach or suggest all of the elements of independent claim 1, which are incorporated into dependent claims 4 and 5. Moreover, as described above, Haugland teaches away from a correction step. Palacios, which Applicants described in their response of April 29, 2009, and which comments are incorporated herein, fails to remedy the deficiencies of Hirao and Haugland. Palacios is merely cited for allegedly describing the standard plants specified in dependent claims 4 and 5.

In view of the above, the combination of Hirao, Haugland, and Palacios fails to teach or suggest all of the elements in dependent claims 4 and 5. Accordingly, withdrawal of the rejection is respectfully requested.

*Claim 7*

Claim 7 is rejected under 35 U.S.C. § 103(a) as allegedly obvious over Hirao in view of Haugland, Palacios, GenBank Accession Number AJ222860, and further in view of Buck *et al.*, *BioTechniques*, 1999, 27:528-536, ("Buck"), *see Office Action*, page 10. Applicants respectfully traverse.

As noted above, Hirao and Haugland fail to teach or suggest all of the elements of independent claim 1, which are incorporated into dependent claim 7. Moreover, as described above, Haugland teaches away from a correction step. As Applicants noted above, Palacios fails to remedy the deficiencies of Hirao and Haugland. Applicants further submit that GenBank Accession Number AJ222860 and Buck do not remedy the deficiencies of Hirao, Haugland, and Palacios. GenBank Accession Number AJ222860 merely discloses the static 18S rRNA, 26S rRNA, ITS-1 and ITS-2 sequences. Buck is merely cited for disclosing an analysis of the effect of a primer design strategy on the performance of DNA sequence primers.

In view of the foregoing, claim 7 is not obvious in view of the cited references. Withdrawal of the rejection is respectfully requested.

### CONCLUSION

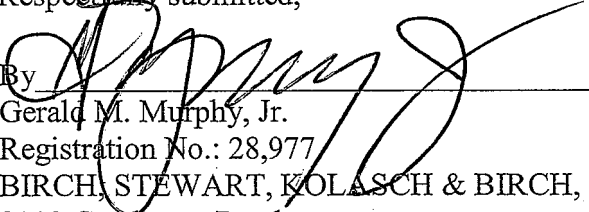
In view of the above, Applicants believe that the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Linda T. Parker, Reg. No. 46,046, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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